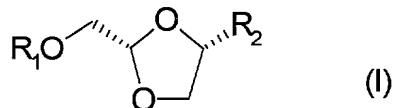


5 CLAIMS:

1. A method of treating a patient having a cancer comprising administering to said patient a compound having the following formula:

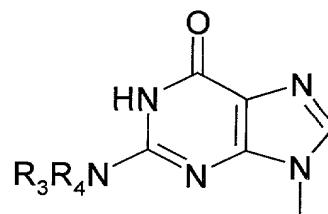
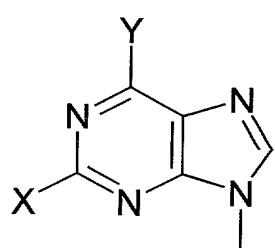
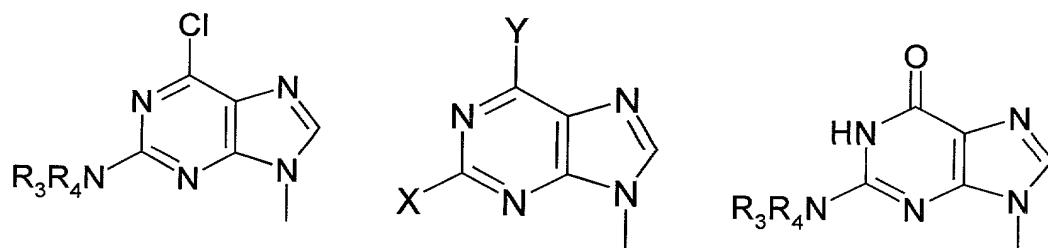
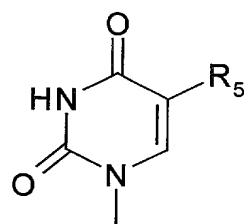
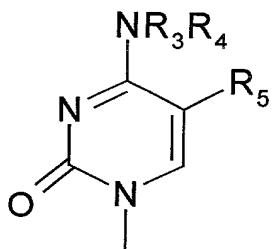
10



wherein:

- 15 R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-20} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$; $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof, wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;
- 20
- 25 R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-18} arylmethyl, C_{2-18} acyloxymethyl, C_{3-8} alkoxy carbonyloxymethyl, C_{3-8} S-acyl-2-thioethyl; saleginyl, t-butyl, phosphate or diphosphate;
- 30
- 35 R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R₂ is



20 R₃ and R₄ are in each case independently H, C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₁₈ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

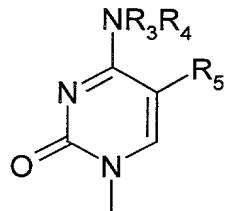
25 R₆ is, in each case, H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₂₄ aryl, C₀₋₂₀ alkyl-C₅₋₂₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S; and

30 R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀ aryl, C₅₋₂₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆, and

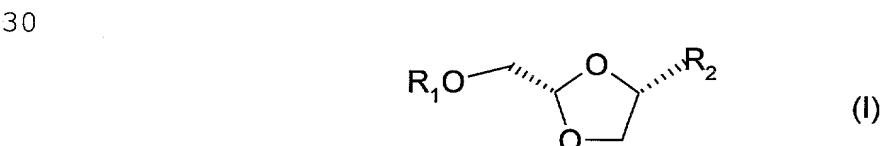
5 X and Y are each independently Br, Cl, I, F, OH, OR₃
 or NR₃R₄ and at least one of X and Y is NR₃R₄; or
 a pharmaceutically acceptable salt thereof.

10 2. A method according to claim 1, wherein at that least
 one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are
 both H and R₁ is -C(O)R₆, -C(O)OR₆ or -C(O)NHR₆, then R₆ is
 other than H.

15 3. A method according to claim 1, wherein R₂ is of the
 formula:



25 4. A method of treating a patient with cancer, wherein
 the cancer cells are deficient in nucleoside or nucleobase
 transporter proteins, comprising administering to said
 patient a compound according to the following formula:



35

wherein:

40 R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₀
 heteroaromatic ring; C₃₋₂₀ non-aromatic ring
 optionally containing 1-3 heteroatoms selected
 from the group comprising O, N, or S; -C(O)R₆;
 -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or
 a dipeptide or tripeptide chain or mimetic

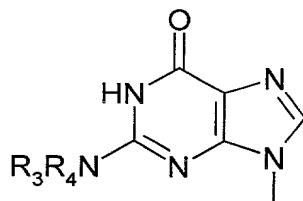
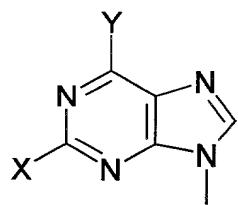
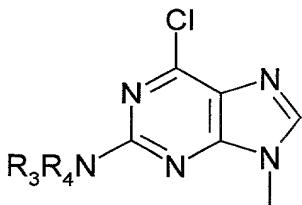
5 thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

10 R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₁₈ arylmethyl, C₂₋₁₈ acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, or C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

15 R₁ can also be monophosphate, diphosphate or triphosphate or mimetics thereof;

20

R₂ is



30 R₃ and R₄ are in each case independently H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₁₈ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn

35

40

5 and Gln, and which in each case is
optionally terminated by -R₇;

10 R₆ is, in each case, H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₀₋₂₀ alkyl-C₆₋₂₄ aryl, C₀₋₂₀ alkyl-C₅₋₁₈ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

15 R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀ aryl, C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected

from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆, and

20 X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof.

5. A method according to claim 4, wherein at least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆, -C(O)OR₆, or -C(O)NHR₆ then R₆ is other than H.

6. A method according to claim 4, wherein said cancer cells are deficient in one or more nucleoside or nucleobase transporter proteins that provide sodium-independent, bidirectional equilibrative transport.

7. A method according to claim 4, wherein said cancer cells are deficient in nucleoside or nucleobase transporter proteins that provide sodium-dependent, inwardly directed concentrative processes.

8. A method according to claim 7, wherein said cancer cells are deficient in nucleoside or nucleobase transporter proteins that provide sodium-dependent, inwardly directed concentrative processes.

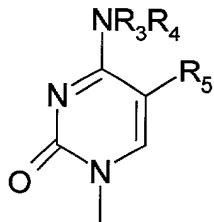
5 9. A method according to claim 4, wherein said cancer cells are deficient in es transporter proteins, ei transporter proteins or both.

10 10. A method according to claim 4, wherein said cancer cells are deficient in cit transporter proteins, cib transporter proteins, cif transporter proteins, csg transporter proteins, cs transporter proteins, or combinations thereof.

15

11. A method according to claim 4, wherein R₂ is of the formula:

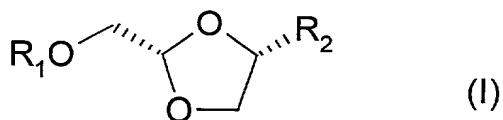
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25

12. A method of treating patients with cancer comprising administering to said patient a compound of the following formula:

30



wherein:

R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gly, and which in each case is optionally terminated by -R₇;

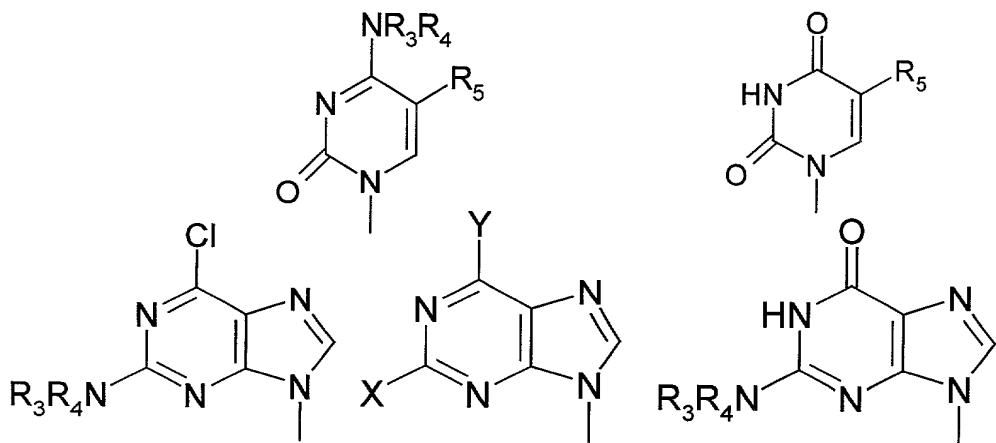
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40

R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₁₈ arylmethyl, C₂₋₁₈ acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R₁ can also be monophosphate, diphosphate, triophosphate or mimetics thereof;

R₂ is



R₃ and R₄ are in each case independently H; C₁₋₂₀ alkyl; C₂₋₂₀ alkenyl; C₆₋₁₀ aryl; C₅₋₁₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile,

5 Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn
 and Gln, and at least one amino acid is not
 Gly, and which in each case is optionally
 terminated by -R₇;

10 R₆ is, in each case, H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₀₋
 20 alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic
 ring, C₃₋₂₀ non-aromatic ring optionally
 containing

15 1-3 heteroatoms selected from the group
 comprising O, N or S;

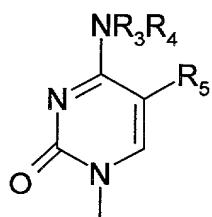
R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀
 aryl, C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ non-aromatic
 ring optionally containing 1-3 heteroatoms
 selected

20 from the group comprising O, N or S, -C(O)R₆,
 -C(O)OR₆, and

X and Y are each independently Br, Cl, I, F, OH, OR₃
 or NR₃R₄ and at least one of X and Y is NR₃R₄;
 with the proviso that least one of R₁, R₃ and R₄ is
 other than H, and if R₃ and R₄ are both H and R₁ is
 -C(O)R₆, -C(O)OR₆, or -C(O)NHR₆ then R₆ is other than
 H; or
 a pharmaceutically acceptable salt thereof;

25 wherein said compound is administered at least daily
 30 for a period of 2 to 10 days.

13. A method according to claim 12, wherein R₂ is of the formula:



- 40 14. A method of treating a patient with cancer wherein
 the cancer is resistant to cytarabine, said method

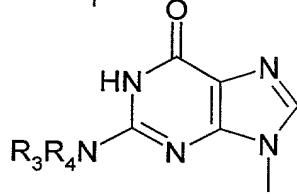
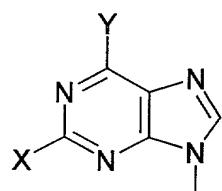
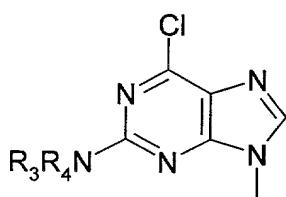
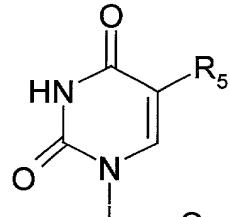
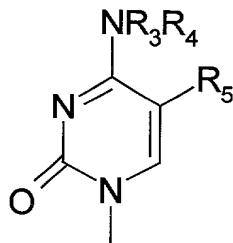
5 comprising administering to said patient a compound according to the following formula:

R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NRH₆; or an amino acid radical or a dipeptide or tripeptide chain or mimetic thereof wherein the amino acids radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

20 R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₁₈ arylmethyl, C₂₋₁₈ acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

25 R₁ can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R₂ is

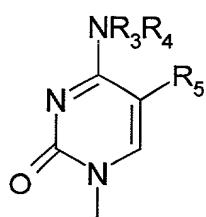


40 R₃ and R₄ are in each case independently H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₁₈

X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof.

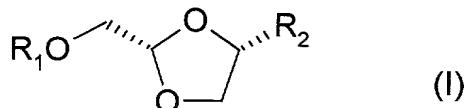
30
15. A method according to claim 14, wherein at least one of R_1 , R_3 and R_4 is other than H, and if R_3 and R_4 are both H and R_1 is $-C(O)R_6$; $-C(O)OR_6$, or $-C(O)NHR_6$ then R_6 is other than H.

35 16. A method according to claim 14, wherein R_2 is of the formula:



17. A method of treating a patient with cancer comprising:

10 determining that a compound enters cancer cells predominately by passive diffusion; and administering said compound to said patient; wherein said compound is a compound according to the formula:



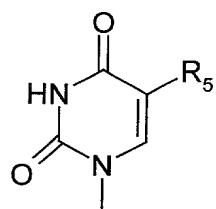
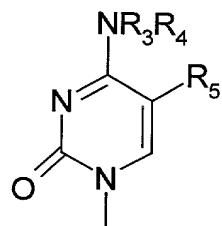
wherein:

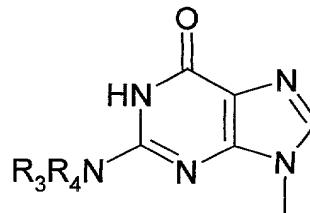
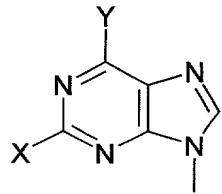
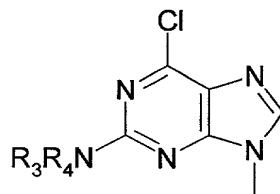
20 R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₄ heteroaromatic ring; C₃₋₂₄ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

30 R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₂₄ arylmethyl, C₂₋₁₈ acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

R₁ can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R₂ is





R₃ and R₄ are in each case independently H; C₂₋₂₄ alkyl; C₁₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₄ heteroaromatic ring; C₃₋₂₄ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

R₆ is, in each case, H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₀₋₂₀ alkyl-C₆₋₂₄ aryl, C₀₋₂₀ alkyl-C₅₋₂₄ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

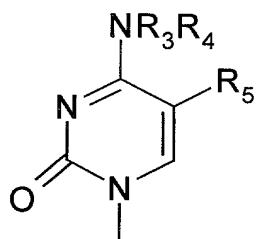
R₇ is, in each case, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₅₋₂₄ heteroaromatic ring, C₃₋₂₀ nonaromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆, and

X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof.

18. A method according to claim 17, wherein at least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆ or -C(O)OR₆, then R₆ is other than H.

5 19. A method according to claim 17, wherein R₂ is of the
formula:

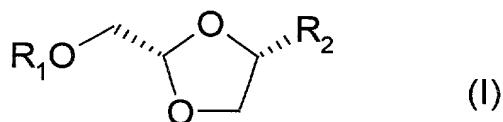
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20. A method of treating a patient with cancer comprising:

15 administering to said patient a compound which has been determined to enter the cancer cells predominately by passive diffusion, wherein said compound is a compound according to the formula:

20



wherein:

25 R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₄ heteroaromatic ring; C₃₋₂₄ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

30

35

R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₇₋₁₈ arylmethyl, C₂₋₁₈ acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

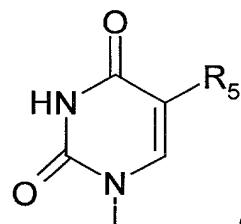
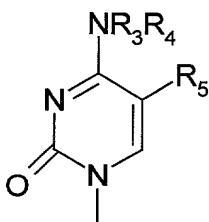
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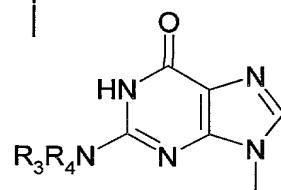
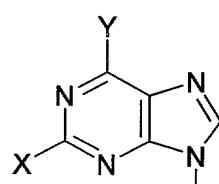
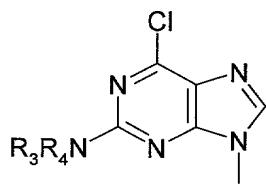
R₁ can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

R₂ is

10



15



20

R₃ and R₄ are in each case independently H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₄ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

25

R₆ is, in each case, H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₀₋₂₀ alkyl-C₆₋₂₄ aryl, C₀₋₂₀ alkyl-C₅₋₂₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

30

R₇ is, in each case, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₅₋₂₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms

35

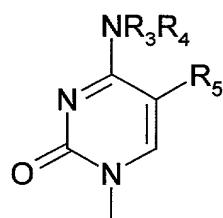
40

5 selected from the group comprising O, N or S,
 $-C(O)R_6$, $-C(O)OR_6$; and

X and Y are each independently Br, Cl, I, F, OH, OR₃
or NR₃R₄ and at least one of X and Y is NR₃R₄; or a
pharmaceutically acceptable salt thereof.

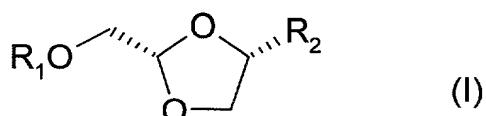
10 21. A method according to claim 20, wherein at least one
of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both
H and R₁ is $-C(O)R_6$; $-C(O)OR_6$ or $-C(O)NHR_6$ then R₆ is other
than H.

15 22. A method according to claim 20, wherein R₂ is of the
formula:



30 23. A method of treating a patient with cancer resistant
to troxacicabine, comprising administering to said patient
a troxacicabine derivative having a greater lipophilicity
than troxacicabine.

35 24. A method according to claim 23, wherein said
derivative is a compound of the following formula:



wherein:

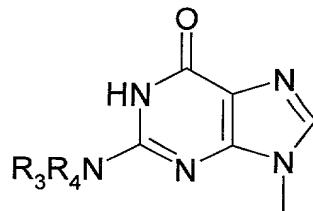
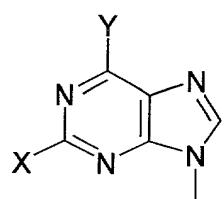
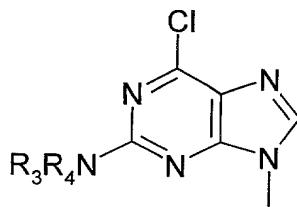
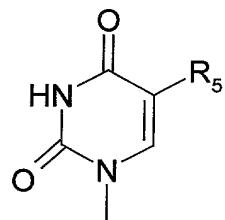
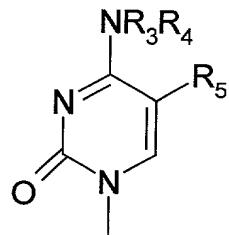
45 R₁ is H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₄
heteroaromatic ring; C₃₋₂₀ non-aromatic ring
optionally containing 1-3 heteroatoms selected
from the group comprising O, N, or S; $-C(O)R_6$;
 $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or

5 dipeptide or tripeptide chain or mimetic thereof
 wherein the amino acid radicals are selected
 from the group comprising Glu, Gly, Ala, Val,
 Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys,
 10 Met, Asn and Gln and the amino acid chain
 contains at least one amino acid other than Gly,
 and which in each case is optionally terminated
 by -R₇;

15 R₁ can also be a P(O)(OR')₂ group wherein R' is in
 each case independently H, C₁₋₂₄ alkyl, C₂₋₂₄
 alkenyl, C₆₋₂₄ aryl, C₇₋₂₄ arylmethyl, C₂₋₁₇
 acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, C₃₋₈
 S-acyl-2-thioethyl, saleginyl, t-butyl,
 phosphate or diphosphate;
 20

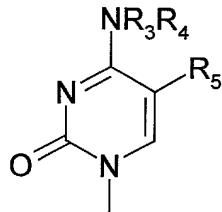
R₁ can also be monophosphate, diphosphate,
 triphosphate or mimetics thereof;

25 R₂ is



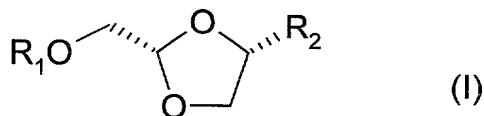
35 R₃ and R₄ are in each case independently H; C₁₋₂₀
 40 alkyl; C₂₋₂₀ alkenyl; C₆₋₁₀ aryl; C₅₋₁₀
 heteroaromatic ring; C₃₋₂₀ non-aromatic ring
 optionally containing 1-3 heteroatoms

- 5 selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln and the amino acid chain contains at least one amino acid other than Gly, and which in each case is optionally terminated by -R₇;
- 10 R₆ is, in each case, H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;
- 15 R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀ aryl, C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆, and
- 20 X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄;
- 25 with the proviso that least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆, -C(O)OR₆ or -C(O)NHR₆, then R₆ is other than H; or
- 30 a pharmaceutically acceptable salt thereof.
- 35 25. A method according to claim 24, wherein R₂ is of the formula:



26. A method of treating a patient with cancer comprising:

determining that a compound does not enter cancer cells predominately by nucleoside or nucleobase transporter proteins; and administering said compound to said patient, wherein said compound is a compound according to the formula:



wherein:

20 R_1 is H; C_{1-24} alkyl; C_{2-24} alkenyl; C_{6-24} aryl; C_{5-20} heteroaromatic ring; C_{3-20} non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; $-C(O)R_6$;

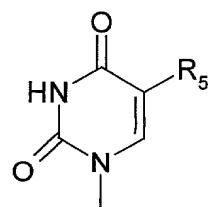
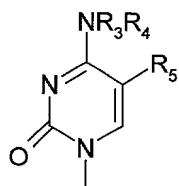
25 $-C(O)OR_6$; $-C(O)NHR_6$; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by $-R_7$;

30 R_1 can also be a $P(O)(OR')_2$ group wherein R' is in each case independently H, C_{1-24} alkyl, C_{2-24} alkenyl, C_{6-24} aryl, C_{7-24} arylmethyl, C_{2-17} acyloxymethyl, C_{3-8} alkoxy carbonyloxy methyl, C_{3-8} S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

35 R_1 can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

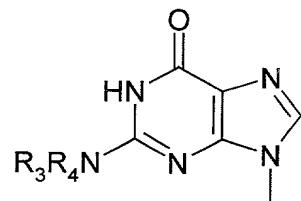
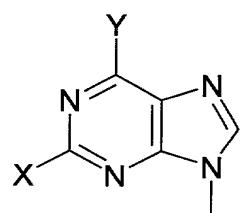
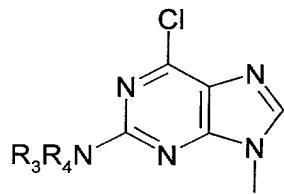
R₂ is

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R₃ and R₄ are in each case independently H; C₁₋₂₄ alkyl; C₂₋₂₄ alkenyl; C₆₋₂₄ aryl; C₅₋₂₄ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NHR₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

30

35

R₆ is, in each case, H, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₀ alkyl-C₆₋₂₄ aryl, C₆₋₂₀ alkyl-C₅₋₂₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

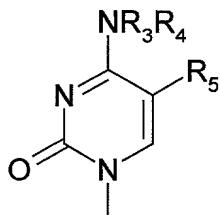
R₇ is, in each case, C₁₋₂₄ alkyl, C₂₋₂₄ alkenyl, C₆₋₂₄ aryl, C₅₋₂₀ heteroaromatic ring, C₃₋₂₀ non-aromatic

5 ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆, and

10 X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof.

15 27. A method according to claim 26, wherein at least one of R₁, R₃ and R₄ is other than H, and if R₃ and R₄ are both H and R₁ is -C(O)R₆, -C(O)OR₆ or -C(O)NHR₆ then R₆ is other than H.

25 28. A method according to claim 27, wherein R₂ is of the formula:



30 29. A method according to any one of claims 1-28, wherein said cancer is prostate cancer, colon cancer, lung cancer, melanoma, ovarian cancer, renal cancer, breast cancer, lymphoma, pancreatic cancer or bladder cancer.

35 30. A method according to any one of claims 3-28, wherein said cancer is leukemia.

40 31. A method according to any one of claims 1-28, wherein at least one of R₁, R₃, or R₄ is piperazinyl, piperidinyl, morpholinyl, pyrrolidinyl, adamantyl or quinuclidinyl.

45 32. A method according to any one of claims 1-28, wherein at least one of R₁, R₃ or R₄ is acetyl, propionyl, butyryl, valeryl, caproic, caprylic, capric, lauric, myristic, palmitic, stearic, oleic, linoleic, or linolenic.

5 33. A method according to any one of claims 1-28, wherein
 at least one of R₁, R₃ or R₄ is cyclopropyl, cyclobutyl,
 cyclopentyl, cyclohexyl, phenyl, napthyl or biphenyl.

10 34. A method according to any one of claims 1-28, wherein
 at least one of R₁, R₃ or R₄ contains a heterocyclic group
 selected from the following group:

15 furyl, thiophenyl, pyrrolyl, imidazolyl, pyrazoyl,
 oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl,
 pyrimidinyl, triazolyl, tetrazolyl, oxadrazolyl,
 thiadiazolyl, thiopyranyl, pyrazinyl, benzofuryl,
 benzothiophenyl, indolyl, benzimidazolyl, benzopyrazolyl,
 benzoxazolyl, benzisoxazolyl, benzothiazolyl,
 20 benzisothiazolyl, benzoxadiazolyl, quinolinyl,
 isoquinolinyl, carbazolyl, acridinyl, cinnolinyl and
 quinazolinyl.

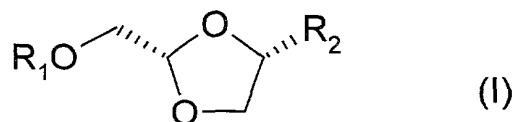
35. A method according to any one of claims 1-28,
 wherein said compound is administered at least daily for a
 period of 2 to 10 days every 2 to 5 weeks.

25 36. A method according to any one of claims 1-28,
 wherein said compound is administered at least daily for a
 period of 2 to 10 days every 3 to 4 weeks.

30 37. A method according to any one of claims 1-28, wherein
 said compound is administered at least daily for 3 to 7
 days every 2 to 5 weeks.

35 38. A method according to any one of claims 1-28, wherein
 said compound is administered at least daily 4 to 6 days
 every 2 to 5 weeks.

39. A compound having the following formula:



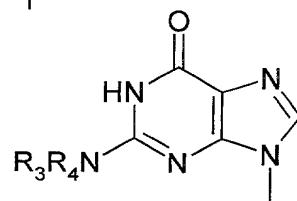
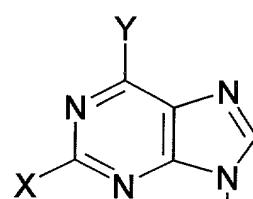
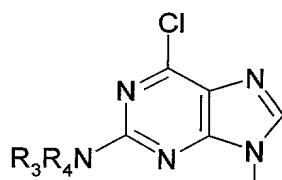
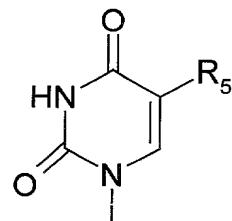
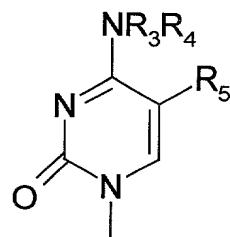
5 wherein:

R₁ is H; C₁₋₂₀ alkyl; C₂₋₂₀ alkenyl; C₆₋₁₀ aryl; C₅₋₁₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NRH₆; or an amino acid radical or dipeptide or tripeptide chain wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Met, Cys, Asn and Gln, and which in each case is optionally terminated by -R₇;

10 R₁ can also be a P(O)(OR')₂ group wherein R' is in each case independently H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀ aryl, C₇₋₁₁ arylmethyl, C₂₋₇ acyloxymethyl, C₃₋₈ alkoxy carbonyloxymethyl, C₃₋₈ S-acyl-2-thioethyl, saleginyl, t-butyl, phosphate or diphosphate;

15 R₁ can also be monophosphate, diphosphate, triphosphate or mimetics thereof;

20 R₂ is



25 R₃ and R₄ are in each case independently H; C₁₋₂₀ alkyl; C₂₋₂₀ alkenyl; C₆₋₁₀ aryl; C₅₋₁₀ heteroaromatic ring; C₃₋₂₀ non-aromatic ring

5 optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S; -C(O)R₆; -C(O)OR₆; -C(O)NRH₆; or an amino acid radical or dipeptide or tripeptide chain or mimetic thereof wherein the amino acid radicals are selected from the group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and which in each case is optionally terminated by -R₇;

10 R₆ is, in each case, H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

15 R₇ is, in each case, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₆₋₁₀ aryl, C₅₋₁₀ heteroaromatic ring, C₃₋₂₀ nonaromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S, -C(O)R₆, -C(O)OR₆; and

20 X and Y are each independently Br, Cl, I, F, OH, OR₃ or NR₃R₄ and at least one of X and Y is NR₃R₄; or a pharmaceutically acceptable salt thereof; with the proviso that at least one of R₁, R₃ and R₄ is

25 C₇₋₂₀ alkyl;
 C₇₋₂₀ alkenyl;
 C₆₋₁₀ aryl;
 C₅₋₁₀ heteroaromatic ring;
 C₄₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N, or S;

30 C(O)R₆ in which R₆ is, C₇₋₂₀ alkyl, C₇₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring, C₄₋₂₀ non-aromatic ring optionally containing 1-3 heteroatoms selected from the group comprising O, N or S;

35 -C(O)OR₆ in which R₆ is C₇₋₂₀ alkyl, C₇₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring, C₄₋₂₀ non-aromatic ring optionally containing 1-3

40 -C(O)OR₆ in which R₆ is C₇₋₂₀ alkyl, C₇₋₂₀ alkenyl, C₀₋₂₀ alkyl-C₆₋₁₀ aryl, C₀₋₂₀ alkyl-C₅₋₁₀ heteroaromatic ring, C₄₋₂₀ non-aromatic ring optionally containing 1-3

5 heteroatoms selected from the group comprising O, N or S;
or

10 a dipeptide or tripeptide or mimetic thereof
where the amino acid radicals are selected from the
group comprising Glu, Gly, Ala, Val, Leu, Ile, Pro,
Phe, Tyr, Trp, Ser, Thr, Cys, Met, Asn and Gln, and
which is optionally terminated by -R₇.

40. A method of treating a patient with cancer comprising
administering to said patient a prodrug form of
15 troxacicabine, having a lipophilic structure to enhance
entry of the prodrug into the cancer cells by passive
diffusion, wherein said lipophilic structure is cleavable
by cellular enzymes, thereby increasing the amount of
20 troxacicabine within the cancer cells to a level greater
than that allowable by administration of troxacicabine in
nonprodrug form.

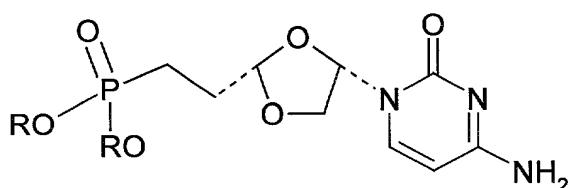
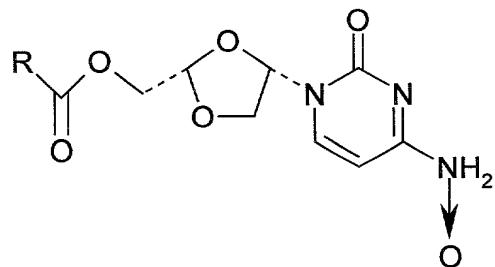
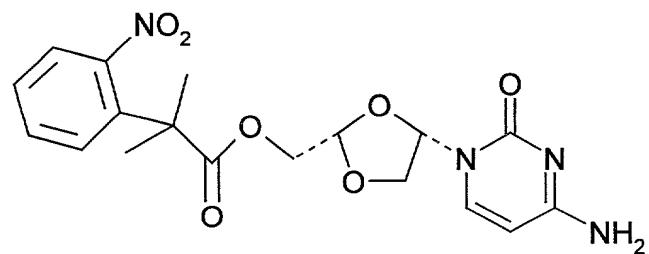
25 41. A method of treating a patient having cancer which is
resistant to gemcitabine, cytarabine or both, comprising
administering to said patient a troxacicabine derivative
having a lipophilic structure which enhances the entry of
the derivative into the cancer cell by the passive
diffusion.

30 42. A method of treating a patient having cancer wherein
the cancer cells are deficient in nucleoside or nucleobase
transporter proteins, comprising administering to said
patient a troxacicabine derivative having a lipophilic
structure which enhances entry of the derivative into the
35 cancer cells by passive diffusion.

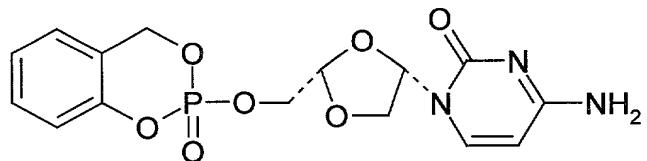
43. A method according to claim 4, wherein said cancer
cells are deficient in one or more nucleobase transporter
proteins.

40

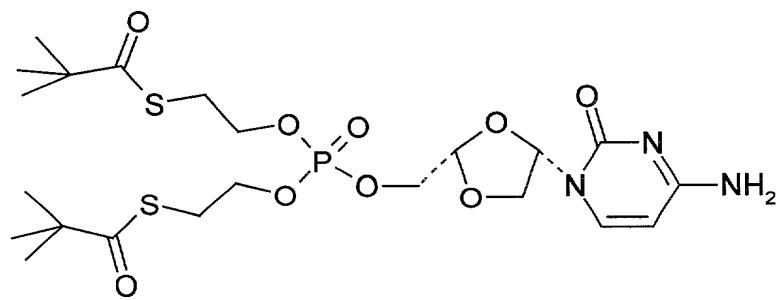
44. A method according to any one of claims 1-28, wherein
the compound is of the formulas



45. A method according to any one of claims 1 to 28 wherein the compound is of the formula



46. A method according to any one of claims 1 to 28, wherein the compound is of the formula



5 46. A method according to any one of claims 1 to 28,
wherein the compound is selected from

4-HEXYL-BENZOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (No. 191) ;

10 8-PHENYL-OCTANOIC ACID [1-(2-HYDROXYMETHYL-[1,3]DIOXOLAN-4-YL)-2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YL]-AMIDE (No. 197) ;

8-PHENYL-OCTANOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (No. 198) ;

15 4-PENTYL-BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (No. 211) ;

4-PENTYL-CYCLOHEXANE CARBOXYLIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (No. 240) or mixtures thereof.

20